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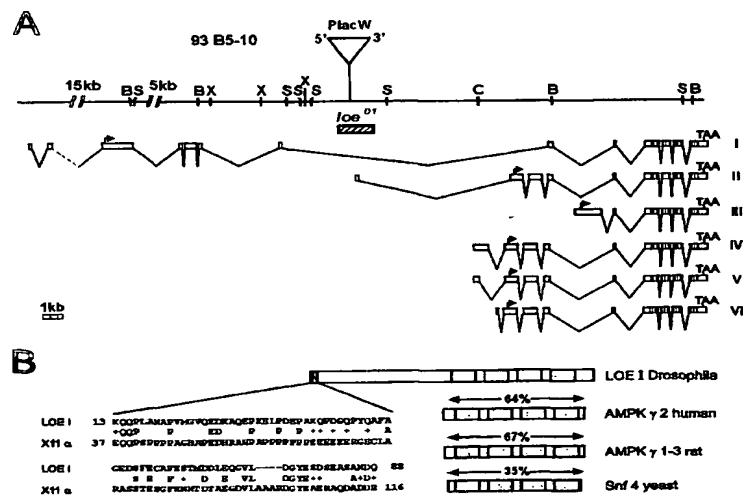
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[Continued on next page]

(54) Title: AN INVERTEBRATE ANIMAL MODEL WITH NEURODEGENERATIVE PHENOTYPE FOR SCREENING AND TESTING SUBSTANCES



(57) Abstract: The present invention claims an invertebrate animal that has been modified to express a set of genes, said set comprising the gene coding for a modified version of the gamma subunit of AMP-activated protein kinase (AMPK γ). According to the invention, the animal displays an identifiable phenotype related to lipid metabolism and neurodegeneration. This animal provides a model of neurodegenerative diseases, particularly Alzheimer's disease, and may be useful for screening and testing modulating agents, substances and therapeutic compounds for neurodegenerative disorders.



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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No

PCT 02/03992

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01K67/033 C12N9/12 C07K14/435 G01N33/50 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C12N C07K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, EMBASE, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TSCHÄPE J-A ET AL: "The Drosophila Mutant Löchrig (loe) - Neurodegeneration and Cholesterol Metabolism" ABSTRACT OF PAPERS PRESENTED AT THE 2001 MEETING ON NEUROBIOLOGY OF DROSOPHILA, October 2001 (2001-10), page 201 XP001170306	1-8, 12-14, 17
Y	the whole document --- -/--	9-11, 15, 16

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

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Date of mailing of the international search report

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FORTINI M E ET AL: "Modeling human neurodegenerative diseases in Drosophila: on a wing and a prayer" TRENDS IN GENETICS, ELSEVIER, AMSTERDAM, NL, vol. 16, no. 4, April 2000 (2000-04), pages 161-167, XP004194020 ISSN: 0168-9525 page 165, paragraph 3 ----	9-11,15, 16
X	WO 01 20003 A (KALM ERNST ;LOOFT CHRISTIAN (DE); AGRONOMIQUE INST NAT RECH (FR);) 22 March 2001 (2001-03-22) claims 6,8,18,19 ----	1,8,12
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E	WO 02 57455 A (SYNGENTA PARTICIPATIONS) 25 July 2002 (2002-07-25) SeqIdNo.63 and 64 ----	1-4
A	DEAK P ET AL: "P-ELEMENT INSERTION ALLELES OF ESSENTIAL GENES ON THE THIRD CHROMOSOME OF DROSOPHILA MELANOGASTER: CORRELATION OF PHYSICAL AND CYTOGENETIC MAPS IN CHROMOSOMAL REGION 86E-87F" GENETICS, GENETICS SOCIETY OF AMERICA, AUSTIN, TX, US, vol. 147, no. 4, December 1997 (1997-12), pages 1697-1722, XP009009475 ISSN: 0016-6731 cited in the application ----	
T	TSCHAEPE JAKOB-ANDREAS ET AL: "The neurodegeneration mutant loechrig interferes with cholesterol homeostasis and APPL processing." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 21, no. 23, 2 December 2002 (2002-12-02), pages 6367-6376, XP002239203 ISSN: 0261-4189 -----	

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 15 and 16, in some respect, are directed to methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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PCT/JP 02/03992

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